

ABSTRACT OF THE DISCLOSURE

[0291] Modified oligonucleotides containing both A-form conformation geometry and B-form conformation geometry nucleotides are disclosed. The B-form geometry allows the oligonucleotide to serve as substrates for RNase H when bound to a target nucleic acid strand. The A-form geometry imparts properties to the oligonucleotide that modulate binding affinity and nuclease resistance. By utilizing C2' endo sugars or O4' endo sugars, the B-form characteristics are imparted to a portion of the oligonucleotide. The A-form characteristics are imparted via use of either 2'-O-modified nucleotides that have 3' endo geometries or use of end caps having particular nuclease stability or by use of both of these in conjunction with each other.